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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/671,040	09/25/2003	Noel J. de Souza	U 014826-4	6697

140 7590 04/07/2005

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EXAMINER

HUANG, EVELYN MEI

ART UNIT PAPER NUMBER

1625

DATE MAILED: 04/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

10/671,040

Applicant(s)

DE SOUZA ET AL.

Examiner

Evelyn Huang

Art Unit

1625

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 13 January 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-7, 22-26, 33, 38 and 43-46 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-7, 22-26, 33, 38, 43-46 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

1. Claims 1-7, 22-26, 33, 38, 43-46 are pending. Claims 8-21, 27-32, 34-37, 39-42 have been canceled according to the preliminary amendment filed on 9-25-2003.

#### ***Claim Rejections - 35 USC § 102(e)***

2. The rejection for Claims 1, 2, 4-7, 38, 43, 44, 46 under 35 U.S.C. 102(e) as being anticipated by De Souza I (6514986) is maintained for reasons of record. Showings to establish that 6514986 is not prior art under 102(e) have not been received.

#### ***Claim Rejections - 35 USC § 102(e)***

3. The rejection for Claims 1, 2, 4-7, 38, 43, 44, 46 under 35 U.S.C. 102(e) as being anticipated by Patel I (2003/0207908, having the application number 09/566875, the US equivalent of WO 00/68229, PTO-1449) or Patel II (6750224, a CIP of 09/566875) is maintained for reasons of record. Showings to establish that 009/566875 or 6750224 is not prior art under 102(e) have not been received.

#### ***Claim Rejections - 35 USC § 102(a)***

4. The rejection for Claims 1, 2, 4-7, 38, 43, 44, 46 under 35 U.S.C. 102(a) as being anticipated by De Souza (WO 01/85095, PTO-1449) is maintained for reasons of record.

Applicants maintain that the reference does not specifically recite the racemate or DL- or D- arginine salts and therefore does not teach each and every elements of the claims.

While the above reference does not specify whether the arginine salt is D or L or is a racemate DL as in the instant claims, it is well known in the art that these are the only 3 possible forms for arginine. The public is therefore in possession of all these forms. The melting point and  $[\alpha]_D^{25}$  recited in the instant claims 22, 24 are physical properties intrinsic to the compound.

***Claim Rejections - 35 USC § 102(b)***

5. The rejection for Claims 1, 2, 4-6, 38, 43, 44, 46 under 35 U.S.C. 102(b) as being anticipated by Patel III (WO 00/68229, PTO-1449) is maintained for reasons of record.

Applicants maintain that the reference does not specifically recite the racemate or DL- or D- arginine salts and therefore does not teach each and every elements of the claims.

While the above reference does not specify whether the arginine salt is D or L or is a racemate DL as in the instant claims, it is well known in the art that these are the only 3 possible forms for arginine. The public is therefore in possession of all these forms. The melting point and  $[\alpha]_D^{25}$  recited in the instant claims 22, 24 are physical properties intrinsic to the compound.

***Claim Rejections - 35 USC § 103***

6. The rejection for Claims 1-7, 21-26, 33, 38, 43-46 under 35 U.S.C. 103(a) as being unpatentable over Ishikawa (4399134, PTO-1449) or Hashimoto (PTO-1449) or Morita (PTO-1449) or Kido (PTO-1449) in view of Berge and/or Fujisawa (3984403, PTO-1449) and further in view of Kwan (5200558, PTO-1449) is maintained for reasons of record.

Applicants maintain that Fujisawa teaches arginine salts of cephalosporins. Cephalosporins have a different core than the compounds of this invention. It is not required that cephalosporins include the benzolijlquinolizine group of the compounds of this invention. Kwan discloses arginine salts of ibuprofen. Ibuprofen like cephalosporins has a different structure than the benzolijlquinolizine compounds of this invention. There is no suggestion or disclosure in Fujisawa and Kwan that arginine salts of benzolijlquinolizine compounds can be prepared. Applicants submit that the Examiner is relying on impermissible hindsight in making this rejection.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the

Art Unit: 1625

applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

In this case, the arginine salts of drug compounds are well known in the art as generically taught by Berge (page 3, column 2, second paragraph). Arginine salts of certain antibacterial compounds of diverse core structures have been shown to lower the toxicity, improve stability and modify the hygroscopicity of the parent drug compound (page 5, Table III). Fujisawa is cited to illustrate the general application to an antibacterial compound and the advantages of its being more stable, more soluble, and causing substantially no pain upon parenteral application (column 1, lines 5-30). Guided by the teaching of Berge and Fujisawa, one of ordinary skill in the art would be motivated to prepare the arginine salt of the piperidiny-benzoquinolizine compound of Ishikawa to arrive at the instant invention with the reasonable expectation of reducing the toxicity while improving stability of the parent drug compound.

It is well known in the art that there are only 3 possible forms for arginine salts for compounds of any core structures: D or L or racemate DL. The public is therefore in possession of all these forms. While the L-arginine is the naturally occurring form, the D-arginine and DL acid are also commercially available. Kwan is cited as an example to illustrate the general application of the D or the L arginine salt of a drug and its advantageous onset-hastened, enhanced response (column 1, lines 40-50). At the time of the invention, guided by the combined teachings of the prior art, one of ordinary skill in the art would be motivated to prepare the D or L or DL arginine salt of the piperidiny-benzoquinolizine compound of Ishikawa to arrive at the instant invention with the reasonable expectation of obtaining an antibacterial compound with enhanced activity.

Art Unit: 1625

7. The rejection for Claims 1-7, 22-26, 33, 38, 43-46 under 35 U.S.C. 103(a) as being unpatentable over Patel III (WO 00/68229, PTO-1449) in view of Kwan (5200558, PTO-1449) is maintained for reasons of record.

Applicants argue that Kwan discloses arginine salts of ibuprofen, which has a different structure than the benzolijlquinolizine compounds of this invention. In addition, there is no suggestion in the combination of the references that the compounds of this invention can be prepared and have the properties described in this application.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

In this case, it is well known in the art that there are only 3 possible forms for arginine salts of compounds of any core structures: D or L or racemate DL. The public is therefore in possession of all these forms. While the L-arginine is the naturally occurring form, the D-arginine and DL acid are also commercially available. Kwan is cited as an example to illustrate the general application of the D or the L arginine salt of a drug and its advantageous onset-hastened, enhanced response (column 1, lines 40-50). At the time of the invention, guided by the combined teachings of the prior art, one of ordinary skill in the art would be motivated to prepare the D or L or DL arginine salt of the piperidinyl-benzoquinolizine compound of Patel III to arrive at the instant invention with the reasonable expectation of obtaining an antibacterial compound with enhanced activity.

### ***Double Patenting***

8. The timely filed terminal disclaimer has obviated the provisional rejection for Claims 1-7, 22-26, 38, 43-46 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-28 of copending Application No. 09/566875 (US 2003/0207908, the US equivalent of WO 00/68229).

Art Unit: 1625

9. The timely filed terminal disclaimer has obviated the rejection for Claims 1, 2, 4-7, 22-26, 38, 43, 44, 46 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-30 of U.S. Patent No. 6514986.

10. The timely filed terminal disclaimer has obviated the rejection for Claims 1-7, 22-26, 33, 38, 43-46 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11 of U.S. Patent No. 6664267.

### ***Conclusion***

11. No claims are allowed.

12. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

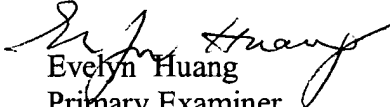
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Evelyn Huang whose telephone number is 571-272-0686. The examiner can normally be reached on Tuesday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecila Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Art Unit: 1625

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
Evelyn Huang  
Primary Examiner  
Art Unit 1625